

Applicants: Herman Jacobus Blok et al.

Appl. No.: 10/579,896

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Amendments to the Claims:

Please cancel Claims 38-51 without prejudice or disclaimer, and amend Claims 1, 6, 11-21 and 29 as set forth below.

1. (Currently amended) A method for screening ~~of cellular responses of~~ viruses, cells or components thereof comprising:

(a) providing a solid porous support having first and second surfaces and at least one area with a plurality of through-going channels;

(b) providing viruses, cells or components thereof ~~cellular components~~ on said first and/or second surface of said solid porous support, wherein said solid porous support retains said viruses, cells or components thereof ~~cellular compounds~~ on its surface, wherein said viruses, cells or components thereof are viruses, mammalian cells, insect cells, yeast cells, fungal cells, plant cells, bacteria, cellular vesicles, cellular organelles, tissue sections, whole organisms or nematodes, or components thereof;

(c) providing a supply chamber at said first and/or second surface and opposite to said cellular components;

(d) subjecting all or part of said viruses, cells or components thereof ~~cellular components~~ to one or more effector molecules ~~effectors~~; wherein at least one effector molecule is delivered from said supply chamber through the porous support, wherein said effector molecules are nutrients, enzyme substrates, test compounds, inducer molecules, chaperone proteins, hormones, oligopeptides, nucleic acids, agonists, antagonists, inhibitors of cellular functions, enhancers of cellular functions, transcription factors, growth factors, differentiation-inducing agents, secondary metabolites, toxins, glycolipids, carbohydrates, antibiotics, mutagens, drugs, proteins, antibodies, antibody fragments, modified analogues thereof, or any combination thereof;

(e) incubating the said all or part of said viruses, cells or components thereof ~~cellular components~~ with said effectors molecules under conditions allowing the

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induction of ~~cellular~~ responses in the said all or part of said viruses, cells or components thereof, ~~cellular components~~ wherein said responses are chemically-induced or physiological events in said cells or viruses; lysis, apoptosis, growth inhibition, growth promotion, morphology changes, cell differentiation, organelle movement, changes in metabolite concentrations or metabolite patterns; changes in cellular contents; changes in mRNA level, protein composition, lipid composition or carbohydrate composition; production, secretion or surface exposure of a protein or a molecule of interest by said cells; membrane surface molecule activation, receptor activation or trans-membrane ion transports; stage of infection to viruses, prions or cellular pathogens or resistance to such pathogens; or cell-cell interactions, or changes to communities or mixtures of cells;

(f) optionally providing detector molecules to the said all or part of said viruses, cells or components thereof ~~cellular components~~ for assaying said ~~cellular~~ responses, wherein said detector molecules are nucleic acids, peptides, proteins, antibodies, antibody fragments, aptamers, enzyme substrates, carbohydrates, or specific dyes and wherein said detector molecules are appropriate to detect responses to be assayed;

(g) assaying for ~~cellular~~ responses using detector molecules, wherein said detector molecules are nucleic acids, peptides, proteins, antibodies, antibody fragments, aptamers, enzyme substrates, carbohydrates, or specific dyes; and

(h) identifying and characterizing the ~~cellular~~ responses induced by said effector molecules.

2. (Previously presented) The method according to claim 1 wherein said supply chamber comprises at least one compartment.

3. (Original) The method according to claim 2, wherein said at least one compartment is provided with a liquid medium comprising at least one effector molecule.

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4. (Previously presented) The method according to claim 2, wherein said at least one compartment is provided with a liquid medium comprising a gradient of at least one effector molecule.

5. (Previously presented) The method according to claim 2, wherein said at least one compartment is provided with a liquid medium comprising a 2D gradient of at least two effector molecules.

6. (Currently amended) The method according to claim 1, wherein said effector molecules are ~~chosen from the group comprising nutrients, enzyme substrates, test compounds, inducer molecules, chaperone proteins, hormones, oligopeptides, nucleic acids, agonists, antagonists, inhibitors of cellular functions, enhancers of cellular functions, transcription factors, growth factors, differentiation inducing agents, secondary metabolites, toxins, glycolipids, carbohydrates, antibiotics, mutagens, drugs, proteins, antibodies, antibody fragments, modified analogues thereof, and any combination thereof.~~

7. (Previously presented) The method according to claim 1, wherein said supply chamber is in liquid contact with said first and/or said second surface of said solid support.

8. (Previously presented) The method according to claim 1, wherein the said at least one effector molecule is transported passively or actively through said porous support.

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9. (Previously presented) The method according to claim 1, wherein the said at least one effector molecule diffuses through said porous support to the cellular components by contact force.

10. (Previously presented) The method according to claim 1, wherein the said at least one effector molecule is transported actively through said porous support by pumping, magnetically, electrically, or by piezo-electronic force.

11. (Currently amended) The method according to claim 1, wherein said providing of viruses, cells or components thereof ~~cellular components~~ on the surface of a support is by a deposit directly on said support of an inoculum, culture, solution, or mixtures thereof.

12. (Currently amended) The method according to claim 1, wherein said cells ~~cellular components~~ are selected from the group comprising mammalian cells or ~~bacteria, insect cells, yeast cells, fungal cells, plant cells, microbial cells, bacterial cells, cellular vesicles, cellular organelles, tissue sections, whole organisms and nematodes.~~

13. (Currently amended) The method according to claim 1, wherein said detector molecules are selected from the group comprising ~~nucleic acids, modified nucleic acid analogues, peptides, modified peptide analogues, oligopeptides, modified oligopeptide analogues, proteins, antibodies, antibody fragments, aptamers, enzyme substrates, carbohydrates, specific dyes, and combinations thereof.~~

14. (Currently amended) The method according to claim 1, wherein said cellular responses are chosen from the group comprising ~~chemically induced or physiological events in the cell, lysis, apoptosis, growth inhibition, growth promotion,~~

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~~morphology changes, cell differentiation, organelle movement, changes in metabolite concentrations or metabolite patterns, changes in cellular contents; changes in mRNA level, protein composition, lipid composition, carbohydrate composition, production of a protein, secretion of a protein, surface exposure of a protein, or other molecule of interest by the cell; membrane surface molecule activation, receptor activation, transmembrane ion transports; stage of infection to viruses, prions or cellular pathogens or resistance to such pathogens; cell-cell interactions, and changes to communities or mixtures of cells.~~

15. (Currently amended) The method according to claim 1, ~~14~~, wherein said molecule of interest is selected from the group consisting of ~~comprising~~ peptides, oligopeptides, lipopeptides, glycosylated peptides, antimicrobial peptides, polypeptides, proteins, enzymes, antimicrobial molecules, primary and secondary metabolites, small organic molecules, pharmaceutical molecules and pharmacophores.

16. (Currently amended) The method according to claim 6, wherein said effector molecule is a drug or ~~any~~ compound which is useful in the discovery process of a drug candidate.

17. (Currently amended) The method according to claim 16, wherein said effector molecule is a drug selected from a chemical or natural drug candidate library.

18. (Currently amended) The method according to claim 1, wherein said ~~cellular~~ response is assayed in whole broth or cell culture medium, in isolated cells, pelleted cells, in supernatant of the cellular components, or in lysate of the cellular components.

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19. (Currently amended) The method according to claim 1, wherein said assaying of ~~cellular~~ responses is by detecting the presence or absence of a change in detectable signal, the presence of a change in detectable signal indicating a ~~cellular~~ response.

20. (Currently amended) The method according to claim 1, wherein delivery of at least one effector molecule is from above the support by a means chosen from the group consisting of ~~comprising~~ a delivery mask, a microfluidics device, a high precision x-y-z micro-pipettor, inkjet printer, and manual handling.

21. (Currently amended) The method according to claim 1, wherein said identifying of the ~~cellular~~ responses is by a method chosen from the group consisting of ~~comprising~~ luminescence, regular light microscopy, and electron microscopy.

22. (Original) The method according to claim 21, wherein said luminescence is fluorescence or phosphorescence.

23. (Previously presented) The method according to claim 1, wherein said solid support is a flow through solid support.

24. (Previously presented) The method according to claim 1, wherein said solid support is a metal oxide solid support.

25. (Original) The method according to claim 24, wherein said metal oxide solid support is an aluminium oxide solid support.

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26. (Previously presented) The method according to claim 1, wherein said assaying is performed in real-time.

27. (Previously presented) The method according to claim 1, wherein said assaying is an end-point assaying.

28. (Previously presented) The method according to claim 1, wherein said cellular components are pre-labelled by introduction of a luminescent indicator.

29. (Currently amended) The method according to claim 1, wherein said detector molecules are present within the pores of the solid support prior to providing said viruses, cells or components thereof ~~cellular components~~ and effecters molecules.

30-54. (Canceled)